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VISCERAL NEW GROWTHS

DR. NORMAN MOORE

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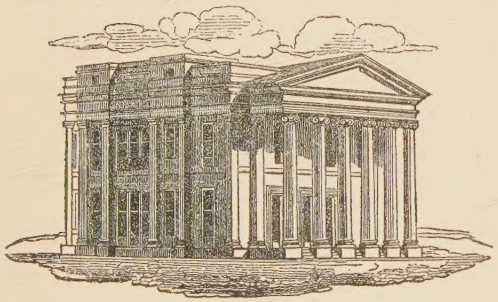

The Royal College of Physicians of London

ON AUGUST 19, 1889

BY

NORMAN MOORE, M.D.

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PATHOLOGICAL ANATOMY OF DISEASES

ARRANGED ACCORDING TO

THE NOMENCLATURE OF DISEASES OF THE ROYAL COLLEGE OF PHYSICIANS OF LONDON

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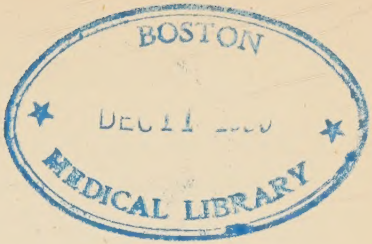

VISCERAL NEW GROWTHS.

Mr. President,—

My first duty is to thank you for doing me the honour to appoint me to lecture on this occasion.

The subject which I have chosen is one on which nothing is to be learned in the medical treastises of ancient times. The Hippocratic writings show that the Greeks had observed that cancer sometimes affected internal organs, that it was a disease of adult life, and that in many cases the cancer continued to grow as long as the patient lived,* but they contain no rules for distinguishing this disease from similar conditions. The physicians of the

* Προῤῥήτικον, ii. 11.

Middle Ages were inclined to neglect observation, but they excelled in definition to such a degree that a reader who goes no further than the first paragraph of their statements on each disease will be inclined to think too well of their knowledge. Dr. John of Gaddesden was the most famous of English physicians before the foundation of this College, and his definition of cancer is: "Cancer est morbus maleficus, tumorem faciens cum duricie, vel ulcerationes faciens cum dolore et fetore et horribilitate."* But his further remarks show that in his time cancer was not exactly distinguished from other forms of tumour, of induration of tissues, and of ulceration. This defect continued for more than four centuries after the time of John of Gaddesden, though a vast collection of observations of new growths of all kinds was made by physicians throughout Europe in consequence of the active study of the morbid anatomy of the human body in its

* Rosa Anglica, Venice, 1516, pp. 125, 126.

relations to clinical medicine, to normal anatomy, and to the anatomy of animals, which was in this country encouraged by your illustrious predecessor, Dr. Caius, and carried on by Harvey, Glisson, Lower, Willis, and many other Fellows of this College. The most famous of them in this part of medicine, Dr. Matthew Baillie, was a contemporary of more than one physician still living. His book, "The Morbid Anatomy of some of the most Important Parts of the Human Body," appeared in 1793, and received improvements from his hand till October 1, 1817, when he sent the fifth edition to the press. This admirable treatise, which is so full of precise and original accounts of what the author had himself seen that it can never become obsolete, contains many observations on new growths. It is easy for any pathologist to satisfy himself that Dr. Baillie was acquainted with the appearances of cancer of the œsophagus, of the stomach, and of the intestine, of the liver, of the pancreas, and of the bladder; with new

growths of the thyroid gland, of the brain, of the lungs, of the ovary, of the peritoneum, and of the pericardium. He had made the observation that such new growths may infect the glands, for he says under the heading "Mesenteric Glands Cancerous" (p. 209): "When a portion of the intestinal canal becomes cancerous, some of the absorbent glands in the mesentery generally become affected with the same disease: this is in consequence of the matter of cancer being conveyed to these glands by absorbent vessels. The glands become enlarged in size, and are changed into hard masses, exhibiting a scirrhous or a cancerous structure." That the defect of definition of cancer from other conditions remained is, however, clear from what Dr. Baillie remarks on "large white tubercle of the liver" (p. 231): "Hard white masses are sometimes found in the liver. They are often as large as a chestnut, but I have seen them both a good deal larger and smaller than this size. They are to be found near the surface of the liver in

greater number than near the middle of its substance; two or three frequently lie contiguous to each other, with a considerable portion of the liver in a healthy state interposed between them and a cluster of similar tubercles. They consist of a firm opaque white substance, and are generally somewhat depressed or hollow upon their outer surface. The liver in this disease is frequently a good deal enlarged beyond its natural size."

"The kind of tubercle which we have now described is much more rare than the other, and resembles more the ordinary appearance of scirrhus in other parts of the body. In one or two instances, however, I have observed a thick sort of pus lodged in this species of tubercle, resembling very much the pus from a scrofulous sore; and therefore I am rather disposed to think that this tubercle may be of a scrofulous nature, but no satisfactory opinion can be formed upon this single circumstance." These tubercles were what we should call masses of carcinoma or of sarcoma,

and we can explain clearly how different are their nature and structure from those of scrofulous sores, to use Dr. Baillie's term. The first step towards the exact definition of the structure of cancer and other new growths was the observation of Leeuwenhoek, in 1674, that the epidermis consisted of minute scales placed side by side. In a letter to Oldenburg he says: "I mentioned that I could not otherwise perceive but that the scarf insensible skin consisted of small round scales, and declared my sense of the skin's fabric thus; that continually as it was worn away on the outside, it was supplied from beneath." *

I do not propose to take up your time with an account of the successive advances in our knowledge of the cellular structure of the skin and of other tissues of the body, and of the gradual abandonment of the word "epidermis" and growth of the use of Ruysch's word "epithelium," from Leeuwenhoek's

* Phil. Trans., 1692–3.

description of the epidermis in 1674 to Waldeyer's enunciation in 1867 of the modern doctrine that carcinoma is a new growth originating in epithelium. But as it is on new growths originating in epithelium that most of my observations have been made, I will ask you at once to consider some well-ascertained facts in its structure and natural history.

An epithelium consists of a continuous surface of nucleated cells, sometimes flat and polyhedral, sometimes columnar in shape, and sometimes with intermediate forms, sometimes in one layer, and sometimes stratified. The cells appear under the microscope almost contiguous, and are held together by a very thin structureless interstitial cement substance. These cells are the descendants of those which at a very early period of life were formed first upon the outer surface of the animal as epiblast, and some of which afterwards as hypoblast came to line the inner surface of the animal. Their ancestors, the

cells of the epiblast and of the hypoblast, having to cover a smaller area, were much fewer in number. They multiplied by division. This power their descendants in the adult epithelium inherit, and thus throughout life as some cells die, and are shed on the surface, fresh cells are formed and take their place. There is what may be called a regular rhythm of growth. If the epithelium is stratified, the cells of the lower layers divide and supply in regular order and interval of time the deficiencies of the superficial layer. If the epithelium is in one layer, similar lateral changes take place in regular rhythm. The cells of the epiblast and of the hypoblast have another peculiarity. Their series can dip down into the subjacent structures and there continue their growth. The epiblast by this kind of ingrowth forms the stomodeum, which in time becomes the cavity of the mouth, and the proctodeum, which becomes the rectum. The hypoblast has numerous ingrowths which become glands. These ingrowths are numerous

and normal in both epiblast and hypoblast. Nowand then they occur at irregular points, as when the epiblast dips in and becomes separated from its original surface and forms one of those dermoid cysts containing teeth and hair which so long confused the ideas of anatomists as to the development of the ovum. This power of ingrowth is not displayed normally after its adult condition is reached. Its cells then proceed to succeed one another in a definite rhythm and along a definite line. The powerful effect of heredity is illustrated by the regularity of their plane and direction of growth. Is it never interrupted? May we not regard a carcinoma as a simple interruption of this regular rhythm of growth? What the disturbing influence is we do not know. Probably it is not always the same. It seems certain that as regularity of growth is a hereditary quality of epithelial cells, so irregularity may also be inherited by some epithelial cells. Thus the cells of every primary carcinoma are normal epithelial cells

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paracentesis performed, and twenty-seven ounces of clear serum were drawn off. The dyspnœa was but little relieved, and three days later the man died. The day afterwards I examined the body. The pericardium contained blood-stained fluid, and both its surfaces were infiltrated with a dense whitish new growth. At the root of the left lung the growth had invaded the main bronchus. The bronchial glands were infiltrated. There was a small nodule on the sixth left rib. Below the diaphragm the growth was only present in the supra-renal bodies. I examined the new growth microscopically in every part in which it occurred, and in all situations it had the same characters. It everywhere consisted of large oval or polyhedral nucleated cells contained in well-marked alveoli. Precisely such cells cover the surface of the pericardium. Obscurity of cardiac sounds was the first physical sign observed. It was followed by pleural effusion, due to the pressure of the growth as it extended from the pericardium

into the lung. The growth on the clavicle was observed to begin to grow some time after the physical signs indicated a growth in the pericardium. Its structure was precisely the same as that of the pericardial growth. No such cells occur in the substance of the supra-renal body, yet the nodule of new growth there had precisely the same cellular appearance as that on the pericardium. I believe the growth to have been primary in the pericardium (1) because the physical signs indicated that new growth began there, (2) because the largest and densest mass of new growth was found involving the pericardium, and (3) because the form and arrangement of the cells of the new growth were identical with those of the normal endothelial cells of the pericardium. As to the growths on the clavicle, in the lung, and in the supra-renal body, their structure was the same as that of the pericardial growth. In the substance of the lung and in the supra-renal body and clavicle no cellular structure exists normally which

is like the structure of the endothelium of the pericardium. The conclusion is obvious that these large polygonal cells grouped together in alveoli in the lung and in the supra-renal body are the descendants of the similar cells of the endothelium of the pericardium. The new growth, due in the pericardium to an alteration of the normal rhythm of growth of the pericardial cells, is in the supra-renal body and lung due to the transference from the pericardium of some of these cells. The pericardium is the mother country of these cells—the masses in the lungs and supra-renal bodies are colonies. I have heard, Sir, that in the midst of your professional labours you have been so wise as to give some of your time to philosophical studies, and I may therefore venture to remind you of a famous passage in which one of the greatest writers and philosophers which this country has produced, points out how colonists when they emigrate carry with them to their new abode the part of the character of their original

nation predominant at the time of their emigration. Some of the cells of the endocardium, which is the seat of morbid growth, are carried off by the circulation or in the lymph channels, and form colonies in a region of totally different structure, the supra-renal body, and there illustrate the principle laid down by Burke. They carry with them the power of developing fresh cells of the original form and the tendency, prevalent when they left the pericardium, for these cells to multiply in irregular groups, instead of in a single layer on an extended surface.

The second example, illustrating the relation of descent between a primary new growth and secondary new growths is afforded by a man aged forty-seven, who was first under my care as an out-patient, and afterwards in St. Bartholomew's Hospital, to which he was admitted on August 25, 1888. He died on September 22 in the same year. Three years and five months before his admission his right

eye had been removed by operation for a new growth in it, which proved on examination to be a melanotic sarcoma, growing from the choroid membrane, and containing dark pigmented connective-tissue cells of the kind normally abundant in the capillary part of that membrane. In August 1888, when I saw him first, he had a greatly-enlarged liver. The socket of his right eye was empty, and showed no sign of disease. His left eye was natural. After death, the enlargement of his liver was proved to be due to its infiltration by numerous masses of new growth mainly consisting of dark pigmented connective-tissue cells, precisely resembling those of the capillary part of the choroid membrane, and wholly unlike any normal cellular structure of the liver. Some of the abdominal lymphatics and the kidneys contained similar masses of pigmented sarcoma. Neither kidneys nor lymphatics normally contain any such pigmented connective-tissue. The conclusion is surely obvious that the abnormally-growing

but normally-constructed pigmented connective-tissue cells of these masses in the liver, abdominal lymphatics, and kidneys were the descendants of the original new growth starting in the normal pigmented cells of the choroid. Their colonising ancestors had already left the original mass in 1885. The growth in such a case is sometimes said to recur in such and such a part after an operation for its removal, but the phrase is incorrect. It does not recur. It began in the choroid, and thence started pigmented cells, which were already on their way to other regions when the original growth was extirpated in the eye. It was truly extirpated, for no morbid change except atrophy of the root of the right optic nerve was discoverable in the head. If I may again borrow an illustration from history, I would compare the melanotic growth in the liver—surviving and flourishing long after the destruction of the original seat of its cells in the choroid—to the Parsi community of Bombay, which pre-

serves in a colony the race and beliefs of a Persian empire destroyed centuries ago by the Mussulman armies.

A third example of the relation of the secondary nodules of a new growth to the primary new growth is that of a man aged fifty-two, who was a patient of Dr. Gee in St. Bartholomew's Hospital, and whom I had the opportunity of observing in the wards and in the post-mortem room. He died of carcinoma of the uppermost part of the rectum growing from the epithelium lining the small crypt-like glands of the mucous membrane. The epithelial cells of these glands are columnar, and they arrange themselves in conformity with the shape of the glands in circular or ovoid tubules. The primary growth had infiltrated the submucous tissue, and consisted entirely of perfectly and imperfectly developed columnar epithelium, arranged exactly as is the normal epithelium of the tubular glands of this part of the rectum. Before death, several nodules had grown so as to be

felt on the surface of the liver through the abdominal wall. After death, many such were found in both lobes of the liver. These masses in microscopic sections showed the columnar cells and tubular arrangements which I have already described as found in the new growth in the rectum. Just as the cells like those of the pericardial endothelium found forming a mass in the supra-renal body, and as the pigmented cells of the choroid kind found in masses in the liver, are, from their resemblance to those of their original seat, and dissimilarity to any cells of the organ in which they were found, believed to be secondary and descended growths, so these columnar epithelial cells arranged in tubules occurring in the liver are to be regarded as secondary to and descended from the primary abnormal growth of the normal columnar epithelium of the tubular glands of the rectum.

It would be easy to multiply examples. I have chosen these three because in each case the clinical history pointed to the new growth

having begun in a particular region, and because the microscopic character of the cells of the region of origin were well marked, peculiar, and unmistakable. I wish these examples to illustrate the law that malignant new growths have a primary seat in which the abnormal growth of normal epithelial cells begins, and that the cells of all secondary growths are descended from these. The microscopic characters alone are, however, not always, as they were in these three cases, sufficient, when studied with the clinical history, to establish after death the position of the primary growth. When these, taken together, leave the determination of the primary growth uncertain, it may be usually settled by a consideration of the naked-eye characteristics of the several parts of the growth. If the growth has been comparatively slow, then the densest mass is probably the oldest. If the growth has been rapid, then the oldest mass will probably be that which is softest, in which most degeneration has taken

place. It is essential, in the investigation of this point, always to consider together these three circumstances—microscopic structure, naked-eye appearance, and clinical history. The growth into the substance of an organ of a carcinoma or sarcoma always gives rise to the formation of fresh connective tissue. When the growth is slow, much connective-tissue formation is present, and the growth is dense. When the growth is rapid, but little connective tissue is formed. Bearing this in mind, the enlargement of lymphatics near the growth must not be taken as a proof that the new growth itself has begun in them; their enlargement is frequently due to simple inflammation. In the same way, it is important, by examining numerous microscopic sections, to guard against the error of mistaking the round cells of the inflammatory process, which are often very abundant round the growth, for the cellular structure of the growth itself. The extensive degeneration which often takes place in the epithelial cells

of a new growth on the surface of a mucous membrane adds to the difficulty of determining the nature of the cellular structure of the new growth unless many sections are examined. In the new growths which I am about to mention I have endeavoured to avoid error due to these circumstances. In each case I have examined the body myself, and have observed both the distribution and the naked-eye appearances of the fresh new growth, and have afterwards examined several sections of the primary growth and of the several secondary growths. In nearly every case I have examined microscopically the secondary growth in all places of its occurrence, and I have always done so when the naked-eye appearances left any room for doubt as to whether what seemed a mass of new growth was really so. In a few instances where many organs were the seat of secondary deposit, and where nearly all were successfully examined, accident prevented the examination of some one secondary nodule.

With this altogether unimportant exception, the statements as to the nature of the new growths which I shall mention are all based on full microscopical examination. Although for practical purposes we may often be quite sure of the nature, say, of a carcinoma of the œsophagus, still it seems desirable, in establishing sound premisses from which to deduce conclusions as to the distribution and duration of new growths, to deal with only those cases in which the precise nature of the growth has been determined by microscopic examination. My own contribution is a very small one; but, if similar collections of observations are made, there will be in time a sufficient accumulation for certainty in these important points with regard to visceral new growths: the directions in which they tend to grow, and to what organs in each case they tend to distribute secondary growths from the primary mass, and the duration of this growth—a period of extreme interest, since, so far as the possibilities of our art are at present, we

must admit that it is conterminous with the survival of the patient.

Following the strict method I have described, I have to lay before you the results of the examination of one hundred and twenty-three cases of new growths in the internal organs of the body. Most of my remarks have relation to new growths from epithelium, for of these cases one hundred and two were carcinomata, and twenty-one sarcomata, among which I include growths from endothelium, though some of their characters are so distinct that it is well to keep for them the distinctive term, "endotheliomata." As to terms, I may add that the term, "scirrhus," which in Heberden and all earlier writers was applied to all growing indurations of tissue in soft parts, whether due to new growth or to the process we term "cirrhosis" in the liver and "sclerosis" in the brain, has little value as a pathological term for a new growth. Hardness is a common character of widely-different new growths, and some carcinomata are softer

than some sarcomata. If the term, "scirrhus," is still to continue, it ought to be used as a purely clinical expression for any dense and therefore slow-growing new growth. The terms, "medullary" and "encephaloid," are open to the same objection, and, as they are not useful in clinical observation, it would be well if they could be allowed to drop out of use altogether. All three terms date from a time when the origin of new growths was unknown, and refer to points in their description which are not distinctive of their nature. Every new growth should now be described by mentioning the form of its cells and their arrangement in relation to one another or to any intervening tissue. The term, "epithelioma," may also with advantage fall into disuse, since it has practically become a synonym for carcinoma. A new growth may become adherent to neighbouring structures and grow into them, and this may be termed, "growth in continuity"; or it may give origin to the formation of masses in distant organs,

when these are termed, "secondary growths." It is of considerable importance to observe this distinction, and I shall do so in the account of visceral new growths to which I shall now proceed, beginning with the alimentary canal and its large glands—the liver and the pancreas, and going on to the lungs, heart, and pericardium, spleen and lymphatics, kidney and brain.

The *œsophagus* is a common seat of new growth in men, a very rare one in women. In fifteen cases which I examined I found that the new growth was in all a carcinoma. All had a well-marked stroma. In five the cells contained in the meshes of the stroma were some of them columnar, suggesting that the morbid epithelium in this case was that of the small mucous glands. In the other ten the cells were polyhedral, or rounded, and of flat appearance, and the morbid epithelium was clearly that which forms the general lining of the œsophagus. In none were there any cell nests, such as are common in cancer of the

lip. In four cases the new growth extended from the lower end of the œsophagus into the stomach. In six there was a growth in continuity into one lung. The commonest seat of secondary growth was the liver, in which masses were found in seven out of fifteen cases. Secondary growths occurred in the lungs in five cases, and in the heart in five. In four, growths were found in the kidneys; and in three of those in which there was growth in the heart there was also growth in the kidneys. The pancreas, spleen, and suprarenal body were each affected in one case. The following conclusions are justified :—(1) That in carcinoma of the œsophagus the new growth is rarely confined to the œsophagus ; (2) that it may grow along the œsophagus into the stomach ; (3) that it may grow directly into the lung, and that this is a frequent occurrence ; (4) that it may grow directly into the mediastinal glands ; (5) that it may, though rarely, infiltrate the dorsal vertebræ ; and (6) that it is frequently associated with

widespread secondary growths, of which the commonest seat is the liver, and that, after the liver, the lungs, heart, and kidneys are more often affected than any other viscera. It is worth while to point out, in addition, that the tendency of the new growth to cause adhesion of the œsophagus to the lung sometimes leads to perforation of the œsophagus, the passage of food into the lung, and the patient's death from gangrene of the lung, or from pneumonia, before actual infiltration of the lung by the new growth has taken place.

The *stomach* is a common seat of new growth in both sexes. In twenty-nine cases, eight in women and twenty-one in men, which I examined microscopically, I found the new growth in all to be a carcinoma. Its stroma was always abundant. The cells in twenty-one of these cases were columnar and spheroidal, with intermediate forms, and probably originated in the layer of columnar cells which line the whole stomach, the pyloric

glands, and the peptic glands. In four cases the cells were polyhedral, resembling and probably growing from those which normally occur at the neck of the pyloric and of the peptic glands. Very great degeneration of many of the cells of the new growth was often present, and in a few cases there was copious hæmorrhage into its substance. In twenty-three out of the twenty-nine examples the new growth was densest at the pylorus, and had grown thence in the gastric wall towards the œsophagus, in eleven cases infiltrating the whole gastric wall. In three cases it was most dense, and radiated from what seemed to have been a simple gastric ulcer of long standing. In two the seat of new growth was the cardiac end, and in one the posterior wall only. In one case the growth, densest at the pylorus, had filled the whole gastric wall and extended a little way into the œsophagus. In one case a mass of new growth projected through the pyloric orifice, but in no case was the wall of the duodenum in

the slightest degree affected. Growth from the stomach in continuity into the lymphatics along its edge occurred in seven cases, into the liver in four, into the diaphragm, omentum and mesentery, pancreas and transverse colon in two each, and into the œsophagus, ascending colon, spleen, vertebral column, and vena cava inferior in one each. Secondary growths occurred in the liver in fourteen; in remote lymphatics, such as the lumbar glands, in nine; in the pancreas in six; in the lungs in five; in the peritoneum generally in three; in the kidney in two; in the heart, spleen, and supra-renal in one each. In three cases only the growth did not extend anywhere beyond the stomach. The following conclusions are justified:—(1) That carcinoma of the stomach generally grows from the pylorus towards the cardiac end of the cavity; (2) that the growth is rarely continued into the œsophagus, but more often than into the duodenum; (3) that in about one-fourth of the cases the growth extends directly into the lymphatics,

along one or both curvatures of the stomach, forming dense masses which may often be felt through the abdominal wall; (4) that after these lymphatics, its most frequent seat of growth in continuity is the liver; (5) that it may also grow in continuity, though with less frequency than into the liver, into the diaphragm, omentum and mesentery, pancreas and tranverse colon, and less often still into the ascending colon, spleen, vertebral column, and vena cava inferior; (6) that in two-thirds of the cases there are secondary growths, and that in one-third these are wide-spread, affecting one or more regions; (7) that the commonest seat of secondary growth is the liver, and next to it remote lymphatics, especially the glands in the hilum of the liver, the lumbar and mesenteric glands, and those of the mediastinum; (8) that after these the pancreas and lungs are most often the seat of secondary growth, and with nearly equal frequency; and (9) that secondary growths are rare, but may

also occur (in the order of frequency) in the peritoneum generally, and in the kidney, and least often, and with equal rarity, in the heart, spleen, and supra-renal bodies.

I have examined nine growths in the *colon*, of which four were in the ascending colon, two in the transverse, and three in the descending. As these are purely artificial divisions, I shall treat of the growths as one series. Three were in women, six in men. All were carcinomata. In eight the cells were distinctly columnar. In one, in which the stroma was very dense, I found no well-formed columnar cells, but only spheroidal cells. All had no doubt originated in the columnar-celled epithelium which lines the large intestine and its mucous glands. Two had grown in continuity into the duodenum, two into the abdominal wall, one into the ileum, one into the stomach, and one into the liver. In two, small lymphatics near the intestine contained new growth, but there was no general infiltration of the abdo-

minal lymphatics. The only remote seat of secondary growth was the liver, and that in only one case. The conclusions justified are : (1) That carcinoma of the colon tends to spread by direct continuity, and may thus, according to its situation, penetrate the stomach, duodenum, ileum, or abdominal wall ; and (2) that it rarely has secondary growths, and that when these occur they are commonest in neighbouring lymphatics, and may rarely be found in the liver.

New growths of the lower part of the *rectum* are commonly sent into the surgical wards of a hospital, and it thus happens that nearly all the cases I have examined are of the upper part. They are eight in number, three in women and five in men. All were examples of carcinoma ; in six the cells were columnar, in two polyhedral, and in one I could find only spheroidal cells. The commonest origin of the cell growth was probably the epithelioma of the mucous glands. In the two cases with polyhedral cells the new

growth was nearer the termination of the intestine, one just within the anus, the other a little higher. The one which most certainly belonged to the area of the proctodeum had as widely-spread secondary growths as any, and had them abundantly in the lumbar glands, liver, and pancreas. The other with polyhedral cells had neither growth in continuity nor secondary deposit. The remainder had no growth in continuity, unless in one case in which the peritoneum was adherent over a very small area, and here I found none, though I suspected it. Five were without any external growth. In those which had secondary growths the lumbar glands were infiltrated in two, the liver in three, and the pancreas in one, in which both liver and lumbar glands were also affected. Even on so small a series it is fair to point out: (1) That in carcinoma of the rectum a majority of the cases have neither growth in continuity nor secondary growths; (2) that the lumbar glands and the liver are the

most frequent regions of secondary growth; and (3) that the pancreas is sometimes infiltrated. On reviewing the new growths of the alimentary canal, it is worth note: (1) That the stomach is a more frequent seat of new growth than the œsophagus, and the œsophagus than the colon, and that, notwithstanding its greater length, and therefore greater area of epithelium, the small intestine is the least frequent of all; (2) that new growths of the œsophagus lead to the most widespread secondary growths, and new growths of the colon to the least widespread; and (3) that new growths of the colon have the greatest tendency, perhaps owing to their situation, to grow directly into the other parts of the alimentary canal.

The *gall-bladder* and *large bile-ducts* are a seat of new growth in both sexes, and I have examined ten cases, five in each sex. All were examples of carcinoma. Polygonal and columnar cells, with intermediate spheroidal and sub-spheroidal forms, were present in all

cases, corresponding exactly to the epithelial cells lining the ducts and the gall-bladder. In one case the common duct only was affected. In all the others the duct near the gall-bladder, and the upper part or the whole of the gall-bladder, were the seat of growth. Gall-stones were present in only four of the cases, and in a fifth a dead, partly-calcified hydatid cyst occupied the fundus of the gall-bladder. In six of the cases the growth extended in continuity into the liver substance for a very short distance. In two it grew directly into the wall of the duodenum, and in one of these into the lumbar glands as well. Of secondary growths, the lymphatics were the most frequent seat, especially the glands in the hilum of the liver, the lumbar and the mesenteric glands. In only two cases was there wide general infiltration of the abdominal lymphatics. In three cases there were secondary growths in the lungs; in one only a separate secondary growth in the liver. In one a scattered growth in the peritoneum. In two

cases there was no growth anywhere else. The following conclusions may be stated :— (1) That carcinoma of the gall-bladder and large bile-ducts (generally the common duct) usually grows directly into the liver; (2) that secondary deposits, if present, are not widespread; (3) that their most frequent seat is the abdominal lymphatics, but that they may occur, in order of frequency, in the lungs, the liver, and the peritoneum.

The *liver* is a rare seat of primary new growth. I have examined three, two of them in men. All three were examples of carcinoma. Two had large polyhedral cells, which were jaundiced (though there was no general jaundice), and the third had polyhedral and columnar cells. Those with only polyhedral cells may have begun in the ultimate termination of the bile-ducts or in the liver-cells, the one with some columnar cells a little lower down in the bile-ducts. In one case the growth had extended in continuity into the omentum. There were no secondary

growths except in the nearest lymphatics, and in a lymphatic on the external surface of the pericardium.

Primary new growth in the *pancreas* occurs in both sexes. Of eleven cases which I have examined, six were in men, five in women. All were examples of carcinoma, with spheroidal and columnar cells closely resembling those of the gland. Growth in continuity into the stomach, gall-bladder, and transverse colon was present in one case, and into the duodenum in another, and in a third into the lymphatics in the hilum of the liver. There were secondary growths in seven cases; in the most widespread example in five separate localities. Next to the neighbouring lymphatics the liver was the most frequent seat, and was infiltrated in six cases, the lungs and the kidney in two, and the peritoneum and heart in one each. The conclusions are: (1) That in carcinoma of the pancreas growth in continuity is rare, but may take place into the stomach, gall-bladder, transverse colon, or

duodenum ; (2) that secondary growths are not usually widespread, and that their commonest seat is the liver ; and (3) that they may also occur in the lungs, kidney, peritoneum, and heart. It is worth mention that jaundice was present in all the cases but one.

Primary new growth in the *lungs* may be a carcinoma or a sarcoma. I have examined eleven, ten of them in men. In all, the new growth formed a dense whitish mass, thickest about the root of the lung. In three, the growth was a sarcoma, consisting of densely-packed round cells, without any stroma, and probably growing from the lymphatic glands at the root of the lung. The other eight were carcinomata, with dense stroma, and columnar or spheroidal cells. In these the new growth probably originated in the epithelium of the mucous glands of the bronchi. In the three sarcomata, there was growth in continuity into the bronchial glands, and in one case into the right auricle. The secondary growths

were into the liver and pancreas in two cases, into the brain and supra-renal in one each, and in one into the vertebral column. The distribution of the carcinomata was similar. One grew in continuity into the right auricle; one had penetrated several ribs; one had secondary growths in the brain. There were secondary growths in the pancreas in half the cases; into remote lymphatics in three; into the liver in two; into the supra-renal, kidney, and spleen in one each. In one case only the growth was confined to one lung, and the bronchial glands were not infiltrated. One of the cases illustrated the necessity for minute examination of all details in the investigation of new growths. The patient had sudden right hemiplegia shortly before and up to her death. It seemed probable that a secondary growth had appeared in the brain, as sometimes happens both in carcinoma and in sarcoma of the lung. At the post-mortem examination, I found an embolus plugging the left middle cerebral artery, and microscopic

sections of this embolus showed it to consist of blood-clot only. The fact that a secondary growth may occur in the brain, in new growth in the lung, deserves notice, and the possibility of direct growth into the heart is also remarkable.

All the primary new growths of the *heart* and *pericardium* (only five in number) which I have examined proved to be endotheliomata, consisting of large polyhedral cells, arranged in a well-marked stroma, and so exactly resembling the cells which line the pericardium that there could be no doubt that they were the origin of the growth. Both surfaces of the pericardium were infiltrated. In one of the cases the growth extended to the endocardium. In three there was a continuous growth into one or both lungs. In all but one case, secondary growths were widespread. In all, the mediastinal lymphatics were infiltrated, and in two the lumbar glands. In three, there were secondary nodules in the lungs; in two, there were nodules in the liver; in two in

the spleen; in two in the pancreas; in two in both kidneys; and in two in both supra-renals. In two cases there was a secondary growth on a clavicle. It is, perhaps, not safe to adopt more than two conclusions: (1) That endothelioma of the pericardium may grow directly into the lung; and (2) that its secondary deposits are usually widespread, and may include the liver, pancreas, spleen, kidney, and supra-renal body.

I have seen but one case of new growth primary in the *spleen*. It was a sarcoma of mixed cells, round and elongated without any stroma, and it grew directly into the stomach, diaphragm, and abdominal lymphatics, without any secondary growths.

Two cases of sarcoma primary in the *lymphatics* may be mentioned here. The new growth consisted of small round cells grouped in the meshes of a connective tissue, and was of the variety known as a lympho-sarcoma. It grew in continuity into the outer part of the pericardium in one case, and into the right

lung in the other. There were no remote growths, except a small nodule in the right lung in the example in which the pericardium was infiltrated.

I have only examined four cases of primary new growth in the *kidney*. Three in adults—two men and one woman—were carcinomata, consisting of spheroidal cells arranged in a well-marked stroma, and in one case in circular alveoli like tubules. One was a sarcoma growing from the pelvis of the kidney in a child aged two years and a half; in this case there were no secondary growths. In all the cases one kidney only was affected. The only growth in continuity was in one carcinoma and was into the right supra-renal body. In two of the carcinomata there were growths into both lungs and into the liver, and in these cases the lumbar glands were also infiltrated. In the third carcinoma, that with the tubular arrangement of cells, the growth was confined to the left kidney. In two of the cases a ragged calculus occupied the pelvis of

the kidney. It deserves note that, while in new growth of the heart (whether primary endothelioma or secondary carcinoma), the kidney is sometimes affected, in none of these four cases of new growth in the kidney was the heart affected.

I have examined six cases of primary growth in the *brain*. All were growths of the genus "sarcoma." Three were in the cerebellum, one in the pons Varolii, one in the left cerebral hemisphere, and one in the optic chiasma. In only one was there any secondary growth except in the brain itself, where in two cases there were several. The extra-cerebral secondary growth in this one case was in the right supra-renal body.

I have now mentioned one hundred and fourteen examples of various new growths. In none of these were there any secondary growths in the uterus, ovaries, or testes. I have not accumulated sufficient observations on new growths of the generative system to enter upon that part of the subject. It is,

moreover, one in which the difficulty of determining precisely the primary growth and its nature is often very great, owing to the rapid and extensive degeneration which often takes place. I have also omitted, as requiring larger discussion than this lecture permits, cases of widely-spread and rapidly-growing sarcoma in children, sometimes involving the skeleton, and sometimes almost all tissues but the bones. It remains to consider the duration of the new growths I have described. In each case I have taken from my own note-book when I had seen the patient during life, and from the careful records written from day to day by the house-physicians at St. Bartholomew's Hospital, when I had not, the date of the first unequivocal symptom of new growth —as, for example, in cancer of the œsophagus, dysphagia ; in cancer of the pancreas, jaundice This clearly does not indicate the beginning of the disease, but it does mark the commencement of its distinct symptoms, and generally the time at which a physician is first likely

to see it. In some of the cases I was unable to determine the duration. I shall mention the longest duration I could make out, and the shortest duration, and the duration of the majority of cases.

In carcinoma of the *œsophagus*, the majority of cases terminated within eight months, the longest case lasted thirteen months, and the shortest two months. In carcinoma of the *stomach* the majority of cases (in both sexes) lasted more than nine months, and half the cases from nine to eighteen months. The evidence seemed conclusive that one case (the longest) lasted sixty months, and another thirty-six months; but these were the only ones which exceeded eighteen months. The shortest case lasted four months, and nearly a quarter of the cases lasted less than six months. In carcinoma of the *colon* the majority of cases lasted from ten months to nineteen months, which was the longest duration, and the shortest duration was four months. In cancer of the *rectum* the majority of cases

lasted from four months to six months. The longest duration was thirteen months, the shortest three months. The duration of the three cases of cancer of the *liver* was respectively ten, seven, and five months. In cancer of the *pancreas* the majority of cases lasted from five to seven months; the longest lasted twelve months, and the shortest five weeks. In carcinoma of the *lung* a majority of cases lasted from seven to nine months, which was the longest duration; the shortest duration was three months. In the three cases of sarcoma of the lung the duration was respectively twelve months, ten months, and five months. In endothelioma of the *heart* and *pericardium* I could not satisfactorily determine the duration in most of the cases. In two which I observed throughout, it was about six months. In the single case of sarcoma of the *spleen*, the patient was under my own observation, and his illness lasted seven months. The two cases of lympho-sarcomata of the *lymphatics* each lasted two months.

In carcinoma of the *kidney*, the longest duration was nine months, the shortest six months. In the sarcomata of the *brain*, the duration of the majority of cases was from one to three months—the longest duration; and the shortest duration was four weeks. The large majority of cases of new growth in the viscera thus seem to terminate within a year from the appearance of distinct symptoms. In some cases, a period of doubtful health preceded the onset of undoubted illness, but this period I found so difficult to define that, as a safer assistance in determining the true duration of growth, I have drawn up a table of nine cases of what may be called external new growth (removed wholly or partially by operation). These show longer periods of time. Seven of them were cancers of the breast. A majority of the patients lived for from twenty-four to fifty-one months, and the shortest duration recorded was fifteen months. A man whose eye had been removed for melanotic sarcoma lived for forty-two months. The secondary

growths in all the cases of carcinoma were widely distributed. Out of seven, the liver was infiltrated in five, the lung in four, the kidney in three, the spleen in two, and the heart, thyroid, and brain in one each. If it be supposed that, after the operation, only a very few morbid epithelial cells remained in the body, we have here a measure of how long they take to grow to a wide distribution—a period ranging from fifteen to fifty-one months. The intermediate durations are sufficiently near to make the mean a useful quantity. It is very nearly twenty-six months; or, omitting the single case of fifty-one months, somewhat more than twenty-one months. If this period be added to that determined by the symptoms, it seems likely that it may give an approximation to the true duration of the disease. For practical purposes, however, the determination of the observable period is far more important, and, in every inquiry which we make as physicians, practical usefulness to sick men ought to be our chief aim.

I hope that the observations recorded in this lecture, and the conclusions based upon them, are likely to be of use in diagnosis, as aiding in determining the probable situation and nature of internal new growths; in therapeutics, since treatment can only be safely based on an accurate diagnosis; and most, perhaps, in prognosis. In the Hippocratic writings, prognosis not only means the prediction of the event, but the prevision of the course of a disease, and of all the probable incidents and opportunities of treatment likely to occur. I have tried to make this lecture a contribution to prognosis in this wider sense. The prognosis of our day is better than that of the Greeks, for it includes among its premisses the sure observations of morbid anatomy, and if Hippocrates could survey the practice of medicine as it now exists, I do not doubt that he would adhere to the opinion he expressed so many ages ago—that the most important thing for a physician is that he should practise forethought, and always have

before his mind what has happened, what is happening, and what will happen in the case which he is treating. *Τὸν ἰητρὸν δοκέει μοι ἄριστον εἶναι πρόνοιαν ἐπιτηδεύειν.*

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